"Nonsense linker" hits

? t s13/7/1-4

13/7/1
DIALOG(R)File 155:MEDLINE(R)

09915995 98343715 PMID: 9680121
The UL4 gene of herpes simplex virus type 1 is dispensable for latency, reactivation and pathogenesis in mice.
Jun P Y; Strelow L I; Herman R C; Marsden H S; Eide T; Haarr L; Leib D A
Department of Ophthalmology and Visual Sciences, Washington University School of Medicine, St Louis, MO 63110, USA.
Journal of general virology (ENGLAND) Jul 1998, 79 (Pt 7) p1603-11, ISSN 0022-1317 Journal Code: 0077340
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Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
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The UL4 gene of herpes simplex virus type 1 is predicted to encode a 21.5 kDa protein of 199 amino acids. Although UL4 is dispensable for growth in cell culture, its function is not known. In the present study, the promoter of UL4 was examined and found to contain a cAMP-response element which bound the transcription factor CREB, and was strongly activated by cAMP. A recombinant virus, termed UL4HS, was constructed with a nonsense linker inserted into the UL4 open reading frame, to make a truncated UL4 protein of 60 amino acids. In addition, a marker-rescued virus, UL4HSMR, was constructed. Western immunoblot analysis revealed a 23 kDa band in extracts of wild-type and marker-rescued virus infected cells which was missing for UL4HS. Only modest differences were observed in the abilities of wild-type and UL4-mutant viruses to grow in Vero cells or in contact-inhibited mouse C3H/10T1/2 cells. In addition, there were only modest differences between the ability of UL4HS to replicate in murine corneas and trigeminal ganglia relative to wild-type viruses, and reactivation of UL4HS from latency was unaffected. Taken together, these data demonstrate that UL4 is dispensable for latency and pathogenesis in mice.
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13/7/2
DIALOG(R)File 155:MEDLINE(R)

08673438 96013772 PMID: 7474089
Role of the virion host shutoff (vhs) of herpes simplex virus type 1 in latency and pathogenesis.
Strelow L I; Leib D A
Department of Ophthalmology and Visual Sciences, Washington University School of Medicine, St. Louis, Missouri 63110, USA.
Journal of virology (UNITED STATES) Nov 1995, 69 (11) p6779-86, ISSN 0022-538X Journal Code: 0113724
Contract/Grant No.: P30-EY02687; EY; NEI; RO1 EY10707; EY; NEI
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The herpes simplex virus type 1 (HSV-1) UL41 gene product, virion host shutoff (vhs), has homologs among five alphaherpesviruses (HSV-1, HSV-2, pseudorabies virus, varicella-zoster virus, and equine herpesvirus 1), suggesting a role for this protein in neurotropism. A mutant virus, termed UL41NHB, which carries a nonsense linker in the UL41 open reading frame at amino acid position 238 was generated. UL41NHB and a marker-rescued virus, UL41NHB-R, were characterized in vitro and tested for their ability to replicate in vitro and in vivo and to establish and reactivate from latency

in a mouse eye model. As demonstrated by Western blotting (immunoblotting) and Northern (RNA) blotting procedures, UL41NHB encodes an appropriately truncated vhs protein and, as expected for a vhs null mutant, fails to induce the degradation of cellular glyceraldehyde-3-phosphate dehydrogenase mRNA. The growth of UL41NHB was not significantly altered in one-step growth curves in Vero or mouse C3H/10T1/2 cells but was impaired in corneas, in trigeminal ganglia, and in brains of mice compared with the growth of KOS and UL41NHB-R. As a measure of establishment of latency, quantitative DNA PCR showed that the amount of viral DNA within trigeminal ganglia latently infected with UL41NHB was reduced by approximately 30-fold compared with that in KOS-infected ganglia and by 50-fold compared with that in UL41NHB-R-infected ganglia. Explant cocultivation studies revealed a low reactivation frequency for UL41NHB (1 of 28 ganglia, or 4%) compared with that for KOS (56 of 76, or 74%) or UL41NHB-R (13 of 20 or 65%). Taken together, these results demonstrate that vhs represents a determinant of viral pathogenesis.

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13/7/3
DIALOG(R)File 155:MEDLINE(R)

07910497 94047367 PMID: 8230470

The herpes simplex virus type 1 regulatory protein ICP0 enhances virus replication during acute infection and reactivation from latency.

Cai W; Astor T L; Liptak L M; Cho C; Coen D M; Schaffer P A

Division of Molecular Genetics, Dana-Farber Cancer Institute, Boston, Massachusetts.

Journal of virology (UNITED STATES) Dec 1993, 67 (12) p7501-12, ISSN 0022-538X Journal Code: 0113724

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ICP0 is a potent activator of herpes simplex virus type 1 gene expression in transient assays and in productive infection. A role for ICP0 in reactivation from latency in vivo has also been suggested on the basis of the observation that viruses with mutations in both copies of the diploid gene for ICP0 reactivate less efficiently than wild-type virus. Because the ICP0 gene is contained entirely within the coding sequences for the latency-associated transcripts (LATs), ICP0 mutants also contain mutations in LAT coding sequences. This overlap raises the question of whether mutations in ICP0 or the LATs, which have also been implicated in reactivation, are responsible for the reduced reactivation frequencies characteristic of ICP0 mutants. Two approaches were taken to examine more definitively the role of ICP0 in the establishment and reactivation of latency. First, a series of ICP0 nonsense, insertion, and deletion mutant viruses that exhibit graded levels of ICP0-specific transactivating activity were tested for parameters of the establishment and reactivation of latency in a mouse ocular model. Although these mutants are ICP0 LAT double mutants, all nonsense mutants induced the synthesis of near-wild-type levels of the 2-kb LAT, demonstrating that the nonsense linker did not disrupt the synthesis of this LAT species. All mutants replicated less efficiently than the wild-type virus in mouse eyes and ganglia during the acute phase of infection. The replication efficiencies of the mutants at these sites corresponded well with the ICP0 transactivating activities of individual mutant peptides in transient expression assays. All mutants exhibited reduced reactivation frequencies relative to those of wild-type virus, and reactivation frequencies, like replication efficiencies in eyes and ganglia, correlated well with the level of ICP0 transactivating activity exhibited by individual mutant

peptides. The amount of DNA of the different mutants varied in latently infected ganglia, as demonstrated by polymerase chain reaction analysis. No correlation was evident between reactivation frequencies and the levels of viral DNA in latently infected ganglia. Thus, replication and reactivation efficiencies of ICP0 mutant viruses correlated well with the transactivating efficiency of the corresponding mutant peptides. In a second approach to examining the role of ICP0 in latency, a single copy of the wild-type gene for ICP0 was inserted into the genome of an ICP0- LAT- double mutant, 7134, which exhibits a marked impairment in its ability to replicate in the mouse eye and reactivate from latency.(ABSTRACT TRUNCATED AT 400 WORDS)
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13/7/4
DIALOG(R)File 155:MEDLINE(R)

07883472 94022333 PMID: 8415670
Epstein-Barr virus latent membrane protein 1 is essential for B-lymphocyte growth transformation.
Kaye K M; Izumi K M; Kieff E
Department of Medicine, Harvard Medical School, Brigham and Women's Hospital, Boston, MA 02115.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Oct 1 1993, 90 (19) p9150-4, ISSN 0027-8424 Journal Code: 7505876
Contract/Grant No.: CA47006-06; CA; NCI; IK11CA01568-01; CA; NCI
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The gene encoding latent-infection membrane protein 1 (LMP1) was specifically mutated in Epstein-Barr virus (EBV) recombinants by inserting a nonsense linker after codon 9 or codon 84 or into an intron 186 bp 3' to the latter insertion site. EBV recombinants with the LMP1 intron mutation were wild type for LMP1 expression and for growth transformation of primary B lymphocytes. In contrast, EBV recombinants with the mutations in the LMP1 open reading frame expressed N-terminally truncated crossreactive proteins and could initiate or maintain primary B-lymphocyte transformation only when wild-type LMP1 was provided in trans by a coinfecting, transformation-defective EBV, P3HR-1. These data indicate that LMP1 is essential for EBV-mediated transformation of primary B lymphocytes, that the first 43 amino acids are critical for LMP1's function, and that codon 44-initiated LMP1 does not have a dominant negative effect on transformation.
Record Date Created: 19931110
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Set	Items	Description
S1	25128	DENDRITIC
S2	878537	DT=REVIEW?
S3	340926	VIRUS OR VIRUSES
S4	2330	S1 AND S3
S5	290	S4 AND S2
S6	790710	INFECT?
S7	204	S6 (2N)S1
S8	204	S6 AND S7
S9	15	S5 AND S7
S10	64833	(HERPES? OR HSV)
S11	23	S8 AND S10
S12	2	UL41NHB
S13	4	NONSENSE(W)LINKER?